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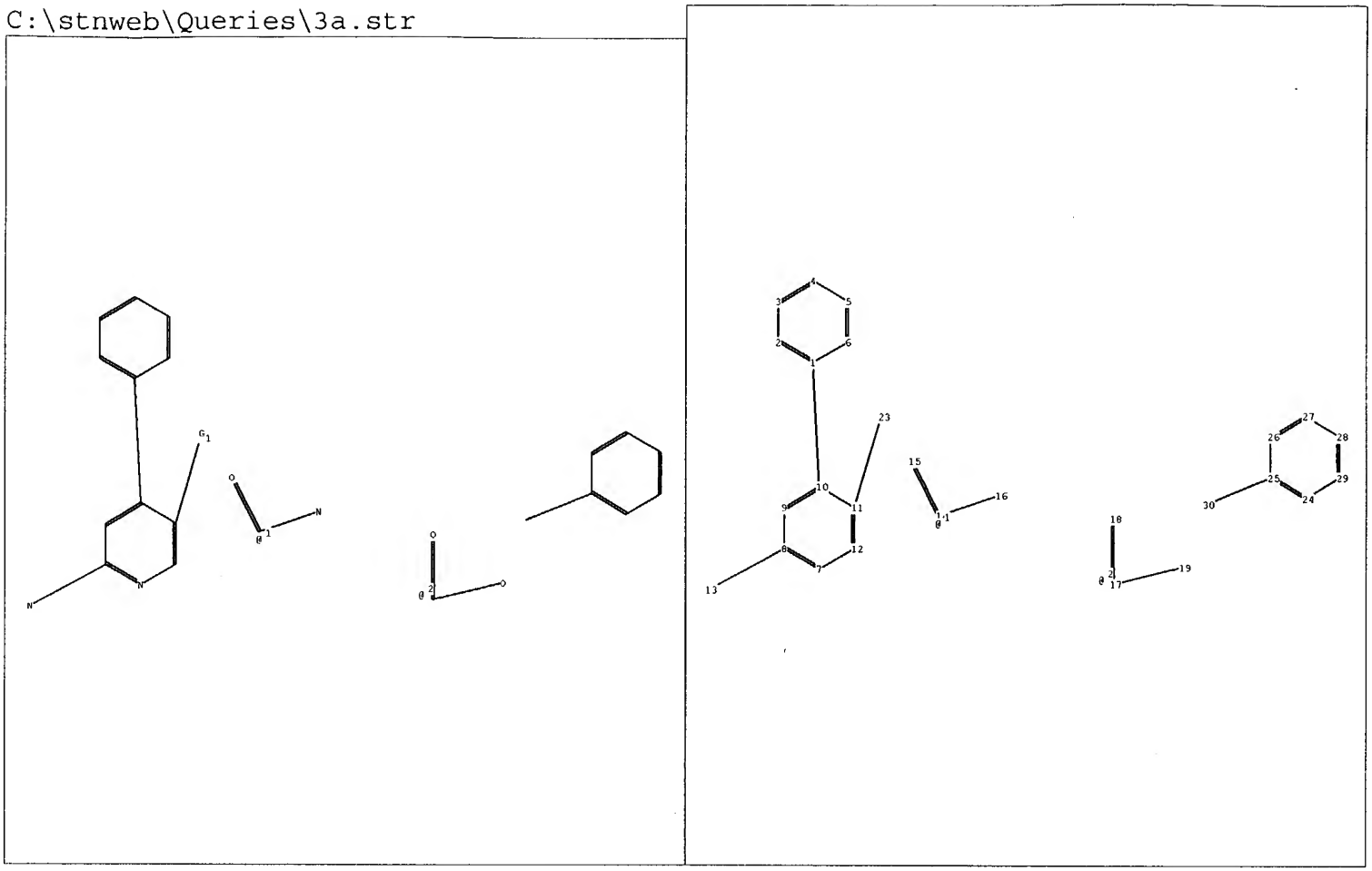

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ring nodes :
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ring bonds :
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24-29 25-26 26-27 27-28 28-29
exact/norm bonds :
8-13 11-23 14-15 14-16 17-18 17-19
exact bonds :
1-10 25-30
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 24-25
24-29 25-26 26-27 27-28 28-29
isolated ring systems :
containing 1 : 7 : 24 :

G1:[*1],[*2]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom
10:Atom 11:Atom 12:Atom 13:CLASS 14:CLASS 15:CLASS 16:CLASS
17:CLASS 18:CLASS 19:CLASS 23:CLASS 24:Atom 25:Atom 26:Atom
27:Atom 28:Atom 29:Atom 30:CLASS

```
* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  JAN 27   Source of Registration (SR) information in REGISTRY updated
                   and searchable
 NEWS  4  JAN 27   A new search aid, the Company Name Thesaurus, available in
                   CA/CAplus
 NEWS  5  FEB 05   German (DE) application and patent publication number format
                   changes
 NEWS  6  MAR 03   MEDLINE and LMEDLINE reloaded
 NEWS  7  MAR 03   MEDLINE file segment of TOXCENTER reloaded
 NEWS  8  MAR 03   FRANCEPAT now available on STN
 NEWS  9  MAR 29   Pharmaceutical Substances (PS) now available on STN
 NEWS 10  MAR 29   WPIFV now available on STN
 NEWS 11  MAR 29   New monthly current-awareness alert (SDI) frequency in RAPRA
 NEWS 12  APR 26   PROMT: New display field available
 NEWS 13  APR 26   IFIPAT/IFIUDB/IFICDB: New super search and display field
                   available
 NEWS 14  APR 26   LITALERT now available on STN
 NEWS 15  APR 27   NLDB: New search and display fields available
 NEWS 16  May 10   PROUSDDR now available on STN
 NEWS 17  May 19   PROUSDDR: One FREE connect hour, per account, in both May
                   and June 2004
 NEWS 18  May 12   EXTEND option available in structure searching
 NEWS 19  May 12   Polymer links for the POLYLINK command completed in REGISTRY

 NEWS EXPRESS  MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
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 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 00:42:09 ON 17 MAY 2004

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

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STRUCTURE FILE UPDATES: 14 MAY 2004 HIGHEST RN 682152-60-9
DICTIONARY FILE UPDATES: 14 MAY 2004 HIGHEST RN 682152-60-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

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Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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L1 STRUCTURE UPLOADED

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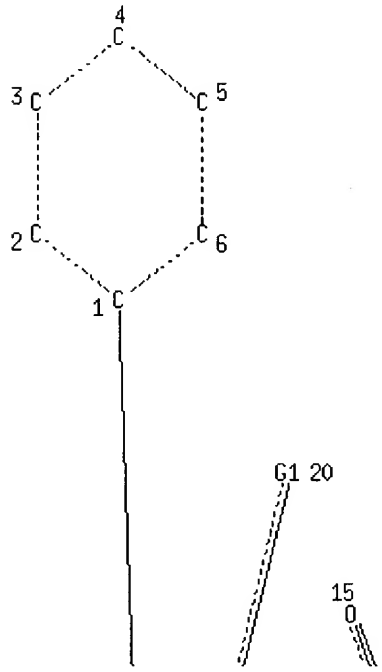
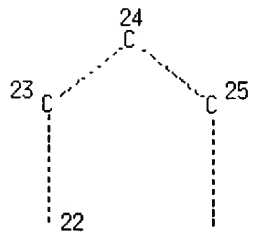
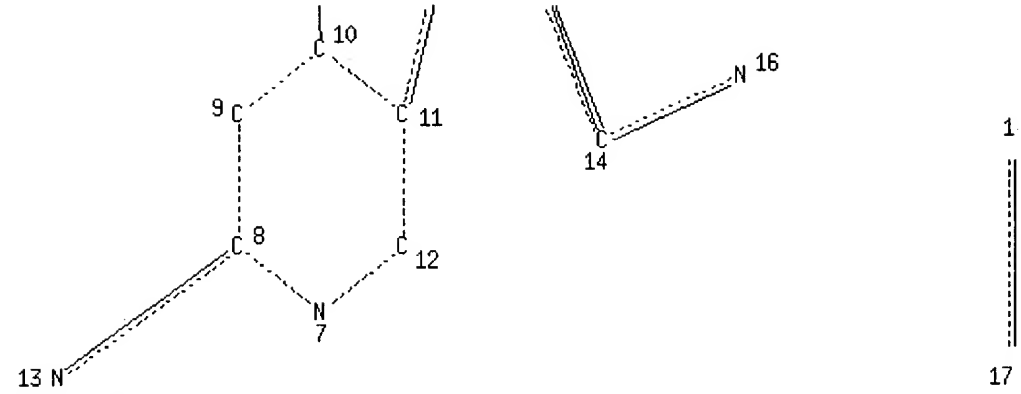
L1 HAS NO ANSWERS
L1 STR



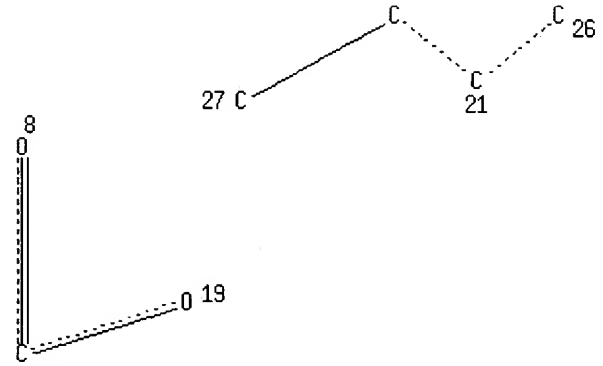
Page 1-A



Page 1-B



Page 2-A



Page 2-B

VAR G1=14/17

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NSPEC   IS R      AT  26
NSPEC   IS C      AT  27
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MLEVEL  IS CLASS  AT  13 14 15 16 17 18 19 27
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  27

STEREO ATTRIBUTES: NONE


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SAMPLE SCREEN SEARCH COMPLETED -     50 TO ITERATE

100.0% PROCESSED      50 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          576 TO     1424
PROJECTED ANSWERS:               0 TO        0

L2             0 SEA SSS SAM L1

=> s l1 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 00:45:01 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    934 TO ITERATE

100.0% PROCESSED     934 ITERATIONS                             11 ANSWERS
SEARCH TIME: 00.00.01

L3            11 SEA SSS FUL L1

=> file hcaplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              157.10     157.31

FILE 'HCAPLUS' ENTERED AT 00:45:05 ON 17 MAY 2004
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FILE LAST UPDATED: 16 May 2004  (20040516/ED)

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 substance identification.
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L4           10 L3

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            301 HOFFMAN, T?/AU
L5            0 L4 AND HOFFMAN, T?/AU

=> s l4 and poli, s?/au
            107 POLI, S?/AU
L6            0 L4 AND POLI, S?/AU

=> s l4 and schnider, p?/au
             33 SCHNIDER, P?/AU
L7            2 L4 AND SCHNIDER, P?/AU

=> d l7, ibib abs fhitstr, 1-2

L7   ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

ACCESSION NUMBER: 2002:90050 HCAPLUS
DOCUMENT NUMBER: 136:134681
TITLE: Preparation of 4-phenylpyridine derivatives as neurokinin-1 receptor antagonists
INVENTOR(S): Hoffmann, Torsten; **Schnider, Patrick**; Stadler, Heinz
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008232	A1	20020131	WO 2001-EP8432	20010720
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002038030	A1	20020328	US 2001-901311	20010709
US 6576762	B2	20030610		
BR 2001012695	A	20030422	BR 2001-12695	20010720
EP 1305319	A1	20030502	EP 2001-960529	20010720
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004504400	T2	20040212	JP 2002-514138	20010720
US 2003130508	A1	20030710	US 2002-282357	20021029
US 6624176	B2	20030923		
NO 2003000353	A	20030123	NO 2003-353	20030123

PRIORITY APPLN. INFO.:

EP 2000-115846	A	20000724
US 2001-901311	A1	20010709
WO 2001-EP8432	W	20010720

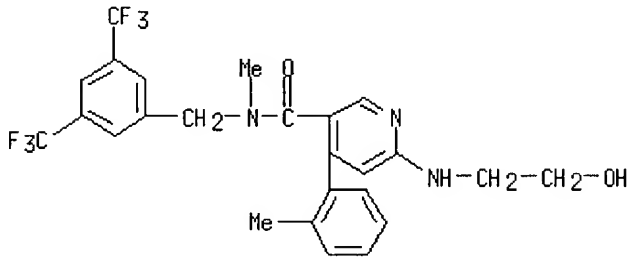
OTHER SOURCE(S): MARPAT 136:134681
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I or II; R1 = III, 2,3-dihydro-[1,4]oxazin-4-yl, imidazol-1-yl, [1,2,4]triazol-1-yl, NH(CH2)2OH, NR3COCH3, NR3COcyclopropyl; R2 = Me, Cl; R3 = H, Me; R = H, (CH2)2OH; n = 1-2] which have a good affinity of the NK-1 receptor and therefore they may be used in the treatment or prevention of diseases, related to this receptor, were prepd. and formulated. E.g., a multi-step synthesis of I [R1 = [1,2,4]triazol-1-yl; R2 = Me] which showed pKi of 8.4 against binding at human NK1 receptors in CHO cells, was given.

IT **393508-71-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 4-phenylpyridines as neurokinin-1 receptor antagonists)

RN 393508-71-9 HCAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[(2-hydroxyethyl)amino]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:607348 HCAPLUS
DOCUMENT NUMBER: 133:207811
TITLE: Preparation of N-benzyl-4-tolylnicotinamides and related compounds as neurokinin-1 receptor antagonists.
INVENTOR(S): Boes, Michael; Branca, Quirico; Galley, Guido; Godel, Thierry; Hoffmann, Torsten; Hunkeler, Walter; **Schnider, Patrick**; Stadler, Heinz
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: Ger. Offen., 38 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10008042	A1	20000831	DE 2000-10008042	20000222

EP 1035115	A1	20000913	EP 2000-102260	20000215
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EP 1394150	A1	20040303	EP 2003-26298	20000215
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GB 2347422	A1	20000906	GB 2000-3908	20000218
NZ 502948	A	20010928	NZ 2000-502948	20000218
FR 2790473	A1	20000908	FR 2000-2170	20000222
FR 2790473	B1	20040402		
US 6297375	B1	20011002	US 2000-507456	20000222
CA 2299139	AA	20000824	CA 2000-2299139	20000223
ZA 2000000894	A	20000824	ZA 2000-894	20000223
NO 2000000885	A	20000825	NO 2000-885	20000223
BR 2000000908	A	20000912	BR 2000-908	20000223
CN 1270959	A	20001025	CN 2000-102401	20000223
HR 2000000097	A1	20011031	HR 2000-97	20000223
ES 2171109	A1	20020816	ES 2000-418	20000223
SG 91856	A1	20021015	SG 2000-1033	20000223
JP 2000247957	A2	20000912	JP 2000-47003	20000224
JP 3399900	B2	20030421		
BG 104187	A	20001130	BG 2000-104187	20000224
AU 767048	B2	20031030	AU 2000-19468	20000224
AU 2000019468	A5	20000831		
US 2002091265	A1	20020711	US 2001-901982	20010710
US 6479483	B2	20021112		

PRIORITY APPLN. INFO.:

EP 1999-103504	A	19990224
EP 1999-123689	A	19991129
EP 2000-102260	A3	20000215
US 2000-507456	A3	20000222

OTHER SOURCE(S): MARPAT 133:207811

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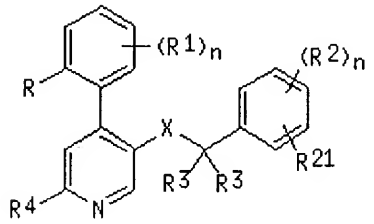


I

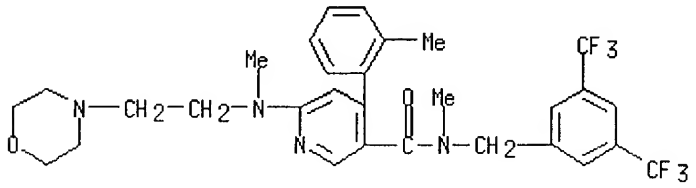
AB Title compds. [I; R = H, alkyl, alkoxy, halo, CF3; R1 = H, halo; RR1 = CH:CHCH:CH; R2, R21 = H, halo, CF3, alkoxy, cyano; R2R21 = (substituted) CH:CHCH:CH; R3 = H, alkyl, cycloalkyl; R4 = H, N(R5)2, N(R5)(CH2)nOH, N(R5)S(O)2A, N(R5)S(O)2Ph, N:CHN(R5)2, N(R5)C(O)R5, specified cyclic tertiary amine; R5 = H, cycloalkyl, benzyl, alkyl; X = C(O)N(R5), (CH2)mO, (CH2)mN(R5), N(R5)C(O), N(R5)(CH2)m; n = 0-4; m = 1, 2], were prepd. Thus, 4-o-tolylnicotinic acid (prepn. given) was stirred with SOCl2 and cat. DMF in CH2Cl2 to give a residue which was refluxed with N-[3,5-bis(trifluoromethyl)benzyl]-N-methylamine and Et3N in PhMe to give 67% N-(3,5-bistrifluoromethylbenzyl)-N-methyl-4-o-tolylnicotinamide. Tested I antagonized NK-1 receptors with pKi = 8.20-9.54.

IT **290296-88-7P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-benzyl-4-tolylnicotinamides and related compds. as neurokinin-1 receptor antagonists)

RN 290296-88-7 HCAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-6-[methyl[2-(4-morpholinyl)ethyl]amino]-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



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(FILE 'HOME' ENTERED AT 00:42:09 ON 17 MAY 2004)

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L2 0 S L1
L3 11 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 00:45:05 ON 17 MAY 2004
L4 10 S L3
L5 0 S L4 AND HOFFMAN, T?/AU
L6 0 S L4 AND POLI, S?/AU
L7 2 S L4 AND SCHNIDER, P?/AU

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L8 8 L4 NOT L7

=> s l8 and sleight, a?/au
460 SLEIGHT, A?/AU
L9 2 L8 AND SLEIGHT, A?/AU

=> s l9 not l7
L10 2 L9 NOT L7

=> d l10, ibib abs fhitstr, 1-2

L10 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:57902 HCAPLUS
DOCUMENT NUMBER: 138:117662
TITLE: Use of NK-1 receptor antagonists for the treatment of brain, spinal or nerve injury
INVENTOR(S): Hoffmann, Torsten; Nimmo, Alan John; **Sleight, Andrew**; Vankan, Pierre; Vink, Robert
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2003006016	A2	20030123	WO 2002-EP7323	20020703
WO 2003006016	A3	20030731		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003083345	A1	20030501	US 2002-187587	20020702
EP 1406618	A2	20040414	EP 2002-764617	20020703

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

PRIORITY APPLN. INFO.: EP 2001-116812 A 20010710
WO 2002-EP7323 W 20020703

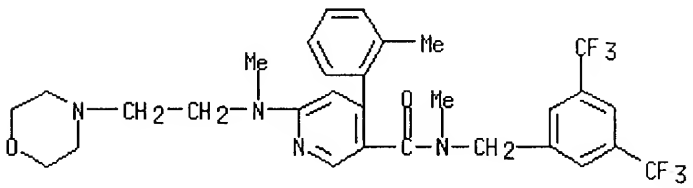
OTHER SOURCE(S): MARPAT 138:117662

AB The invention discloses the use of an NK-1 receptor antagonist (Markush included), e.g. N-(3,5-bis-trifluoromethylbenzyl)-N-methyl-6-(4-methylpiperazin-1-yl)-4-o-tolylnicotinamide, optionally in combination with a magnesium salt, for the treatment and/or prevention of brain, spinal or nerve injury. The invention also relates to pharmaceutical compns. comprising one or more such NK-1 receptor antagonists, optionally in combination with a magnesium salt, and a pharmaceutically acceptable excipient, for the treatment and/or prevention of brain, spinal or nerve injury.

IT 290296-88-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NK-1 receptor antagonist for treatment of brain, spinal or nerve injury)

RN 290296-88-7 HCAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-6-[methyl[2-(4-morpholinyl)ethyl]amino]-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



L10 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

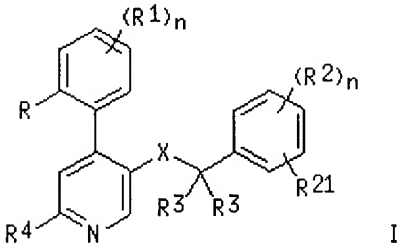
ACCESSION NUMBER: 2002:832668 HCAPLUS
DOCUMENT NUMBER: 137:337901
TITLE: Preparation and use of amides as NK-1 receptor antagonists against benign prostatic hyperplasia
INVENTOR(S): Buser, Susanne; Ford, Anthony P. D. W.; Hoffmann, Torsten; Lenz, Barbara; **Sleight, Andrew John**; Vankan, Pierre
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 45 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085458	A2	20021031	WO 2002-EP1085	20020202
WO 2002085458	A3	20031030		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1385577	A2	20040204	EP 2002-719751	20020202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003004157	A1	20030102	US 2002-71570	20020208

PRIORITY APPLN. INFO.: EP 2001-109853 A 20010423
WO 2002-EP1085 W 20020202

OTHER SOURCE(S): MARPAT 137:337901
GI



I

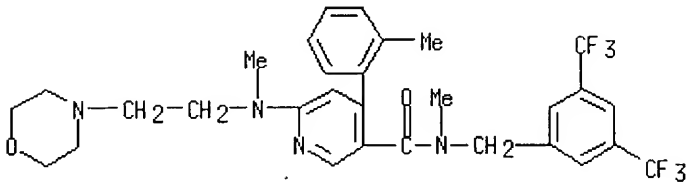
AB Use of an NK-1 receptor antagonist for the treatment or prevention of benign prostatic hyperplasia (BPH) is claimed. The preferred NK-1 receptor antagonists are compds. of the general formula [I; R = H, alkyl, alkoxy, halo, CF3; R1 = H, halo; RR1 = CH:CHCH:CH; R2, R21 = H , halo , CF3, alkyl, alkoxy, cyano; R2R21 = CH:CHCH:CH, optionally substituted by 1-2 alkyl, halo, alkoxy; R3 = H, alkyl; R3R3C = cycloalkyl; R4 = H, N(R5)2, NR5(CH2)nOH, cyclic tertiary amine, etc.; X = CONR5, (CH2)pO, NR5(CH2)p, etc.; R5 = H, cycloalkyl, Ph, PhCH2, alkyl; n = 0-4; p = 1-3]. Preferred compds. are 2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-(6-morpholin-4-yl-4-o-tolyl-pyridin-3-yl)isobutyramide, 3-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-[6-(4-methyl-piperazin-1-yl)-4-o-tolyl-pyridin-3-yl]isobutyramide, 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-4-o-tolyl-pyridin-3-yl]-N-methylisobutyramide, and 2-(3,5-bis-trifluoromethylphenyl)-N-[6-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-4-(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methylisobutyramide. Thus, 2-[3,5-bis(trifluoromethyl)phenyl]-N-methyl-N-(6-thiomorpholin-4-yl-4-o-tolylpyridin-3-yl)isobutyramide (prepn. given) oxone were stirred 2 days at room temp. to give 2-(3,5-bis-trifluoromethylphenyl)-N-[6-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-4-o-

tolylpyridin-3-yl]-N-methylisobutyramide. 2-(3,5-Bistrifluoromethylphenyl)-N-methyl-N-methyl-N-(6-morpholin-4-yl-4-o-tolylpyridin-3-yl)isobutyramide at 60 mg/kg/day orally in dogs reduced prostate wt. by 58% after 39 wk.

IT 290296-88-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. and use of amides as NK-1 receptor antagonists against benign prostatic hyperplasia)

RN 290296-88-7 HCAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-6-[methyl[2-(4-morpholinyl)ethyl]amino]-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)

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=> d hs
'HS' IS NOT A VALID FORMAT FOR FILE 'HCAPLUS'

The following are valid formats:

ABS --------- GI and AB
ALL --------- BIB, AB, IND, RE
APPS -------- AI, PRAI
BIB --------- AN, plus Bibliographic Data and PI table (default)
CAN --------- List of CA abstract numbers without answer numbers
CBIB -------- AN, plus Compressed Bibliographic Data
DALL -------- ALL, delimited (end of each field identified)
DMAX -------- MAX, delimited for post-processing
FAM --------- AN, PI and PRAI in table, plus Patent Family data
FBIB -------- AN, BIB, plus Patent FAM
IND --------- Indexing data
IPC --------- International Patent Classifications
MAX --------- ALL, plus Patent FAM, RE
PATS -------- PI, SO
SAM --------- CC, SX, TI, ST, IT
SCAN -------- CC, SX, TI, ST, IT (random display, no answer numbers;
              SCAN must be entered on the same line as the DISPLAY,
              e.g., D SCAN or DISPLAY SCAN)
STD --------- BIB, IPC, and NCL

IABS -------- ABS, indented with text labels
IALL -------- ALL, indented with text labels
IBIB -------- BIB, indented with text labels
IMAX -------- MAX, indented with text labels
ISTD -------- STD, indented with text labels

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations
```

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HIT --------- Fields containing hit terms
HITIND ------ IC, ICA, ICI, NCL, CC and index field (ST and IT)
              containing hit terms
HITRN ------- HIT RN and its text modification
HITSTR ------ HIT RN, its text modification, its CA index name, and
              its structure diagram
HITSEQ ------ HIT RN, its text modification, its CA index name, its
              structure diagram, plus NTE and SEQ fields
FHITSTR ----- First HIT RN, its text modification, its CA index name, and
              its structure diagram
FHITSEQ ----- First HIT RN, its text modification, its CA index name, its
              structure diagram, plus NTE and SEQ fields
KWIC -------- Hit term plus 20 words on either side
OCC --------- Number of occurrence of hit term and field in which it occurs

To display a particular field or fields, enter the display field
codes.  For a list of the display field codes, enter HELP DFIELDS at
an arrow prompt (=>).  Examples of formats include: TI; TI,AU; BIB,ST;
TI,IND; TI,SO.  You may specify the format fields in any order and the
information will be displayed in the same order as the format
specification.

All of the formats (except for SAM, SCAN, HIT, HITIND, HITRN, HITSTR,
FHITSTR, HITSEQ, FHITSEQ, KWIC, and OCC) may be used with DISPLAY ACC
to view a specified Accession Number.
ENTER DISPLAY FORMAT (BIB):end

=> d his

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L2            0 S L1
L3           11 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 00:45:05 ON 17 MAY 2004
L4           10 S L3
L5            0 S L4 AND HOFFMAN, T?/AU
L6            0 S L4 AND POLI, S?/AU
L7            2 S L4 AND SCHNIDER, P?/AU
L8            8 S L4 NOT L7
L9            2 S L8 AND SLEIGHT, A?/AU
L10           2 S L9 NOT L7

=> s l8 not l10
L11           6 L8 NOT L10

=> d l11, ibib abs fhitstr, 1-6

L11  ANSWER 1 OF 6  HCAPLUS  COPYRIGHT 2004 ACS on STN
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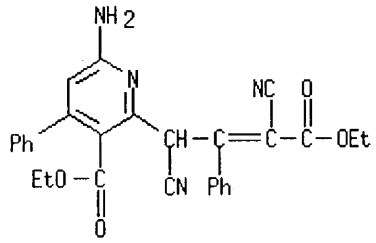
ACCESSION NUMBER:         2000:289701  HCAPLUS
DOCUMENT NUMBER:          133:89415
TITLE:                    β-Enaminonitriles in heterocyclic synthesis:
                          synthesis of new 1,4-dihydropyridine,
                          pyrazolo[1,5-a]pyrimidine, aminothiophene and pyridine
                          derivatives
```

AUTHOR(S): Hafiz, Ibrahim S. A.
CORPORATE SOURCE: Department of Chemistry, Faculty of Education, Suez Canal University, Arish, Egypt
SOURCE: Zeitschrift fuer Naturforschung, B: Chemical Sciences (2000), 55(3/4), 321-325
CODEN: ZNBSEN; ISSN: 0932-0776
PUBLISHER: Verlag der Zeitschrift fuer Naturforschung
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Utility of 3-aminocinnamonitrile in the synthesis of new 1,4-dihydropyridine, pyrazolo-[1,5-a]pyrimidine, aminothiophene and pyridine derivs. is reported.
IT **281195-26-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of dihydropyridine, pyridine, pyrazolo[1,5-a]pyrimidine, aminothiophene derivs. from (amino)(phenyl)propenenitrile)
RN 281195-26-4 HCAPLUS
CN 3-Pyridinecarboxylic acid, 6-amino-2-(1,3-dicyano-4-ethoxy-4-oxo-2-phenyl-2-butenyl)-4-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 1998:545594 HCAPLUS
DOCUMENT NUMBER: 129:148914
TITLE: Preparation of 2-amino-4-aryl-5-arylmethyl-5-cyclopentyl-3-hydroxymethylpyridines and related compounds for treatment of arteriosclerosis.
INVENTOR(S): Schmeck, Carsten; Brandes, Arndt; Loegers, Michael; Schmidt, Gunter; Bremm, Klaus-Dieter; Bischoff, Hilmar; Schmidt, Delf; Schuhmacher, Joachim
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: Ger. Offen., 22 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19704243	A1	19980806	DE 1997-19704243	19970205
WO 9834920	A1	19980813	WO 1998-EP362	19980123

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9862123	A1	19980826	AU 1998-62123		19980123
AU 730109	B2	20010222			
BR 9807181	A	20000125	BR 1998-7181		19980123
EP 973744	A1	20000126	EP 1998-904126		19980123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
NZ 337011	A	20010427	NZ 1998-337011		19980123
JP 2001510478	T2	20010731	JP 1998-533691		19980123
NO 9903738	A	19990917	NO 1999-3738		19990802
BG 103631	A	20001130	BG 1999-103631		19990803
MX 9907244	A	20000131	MX 1999-7244		19990805
PRIORITY APPLN. INFO.:			DE 1997-19704243	A	19970205
			WO 1998-EP362	W	19980123

OTHER SOURCE(S): MARPAT 129:148914

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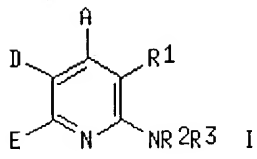

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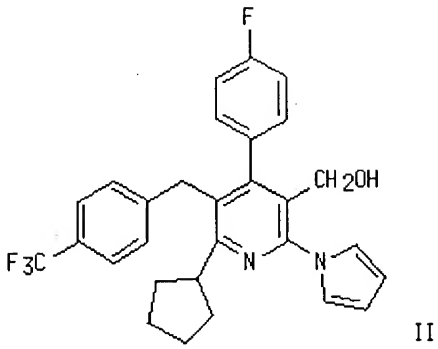


II

AB Title compds. [I; A = (substituted) aryl; D = (substituted) aryl, R6L, etc.; R6 = (substituted) cycloalkyl, aryl, (benzocondensed) mono-, di-, or tricyclic heterocyclyl; L = (substituted) alkyl, alkenyl; E = cycloalkyl, (substituted) alkyl; R1 = hydroxyalkyl; R2, R3 = H, Ph, PhCH2, cycloalkyl, alkyl, acyl, aminocarbonyl; R2R3N = 5-7 membered (unsatd.) (benzocondensed) (substituted) heterocyclyl], were prepd. Thus, title compd. (II) inhibited cholesteryl ester transfer protein with IC50 = 6 × 10-8 M.

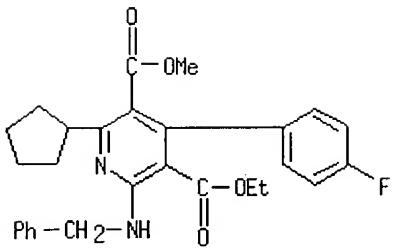
IT **201848-96-6P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of 2-amino-4-aryl-5-arylmethyl-5-cyclopentyl-3-hydroxymethylpyridines and related compds. for treatment of arteriosclerosis)

RN 201848-96-6 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-cyclopentyl-4-(4-fluorophenyl)-6-[(phenylmethyl)amino]-, 5-ethyl 3-methyl ester (9CI) (CA INDEX NAME)



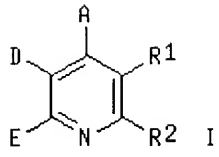
L11 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:55686 HCAPLUS
DOCUMENT NUMBER: 128:128005
TITLE: Preparation of condensed pyridines for treatment of hyperlipoproteinemia and arteriosclerosis.
INVENTOR(S): Schmeck, Carsten; Mueller-Gliemann, Matthias; Schmidt, Gunter; Brandes, Arndt; Angerbauer, Rolf; Loegers, Michael; Bremm, Klaus-Dieter; Bischoff, Hilmar; Schmidt, Delf; Schuhmacher, Joachim
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: Ger. Offen., 44 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19627431	A1	19980115	DE 1996-19627431	19960708
EP 818197	A1	19980114	EP 1997-110361	19970625
EP 818197	B1	20031112		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 253911	E	20031115	AT 1997-110361	19970625
US 5932587	A	19990803	US 1997-883673	19970627
JP 10167967	A2	19980623	JP 1997-192014	19970703
AU 715101	B2	20000113	AU 1997-28449	19970703
AU 9728449	A1	19980115		
CA 2209825	AA	19980108	CA 1997-2209825	19970704
TW 382631	B	20000221	TW 1997-86109414	19970704
IL 121234	A1	20001206	IL 1997-121234	19970704
NO 9703143	A	19980109	NO 1997-3143	19970707
ZA 9706020	A	19980202	ZA 1997-6020	19970707
CN 1174196	A	19980225	CN 1997-114562	19970708
BR 9703890	A	19981103	BR 1997-3890	19970708
PRIORITY APPLN. INFO.:			DE 1996-19627431 A	19960708
			DE 1996-19627432 A	19960708

OTHER SOURCE(S): MARPAT 128:128005
GI



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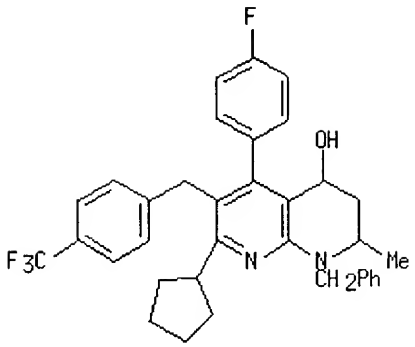


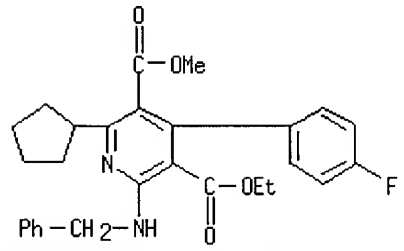
II

AB Title compds. [I; A = (substituted) aryl; D = R5X, R6R7R8C; R5, R6 = cycloalkyl, (substituted) aryl, benzocondensed heterocyclyl; R7 = H, halo; R8 = H, halo, N3, CF3, OH, OCF3, alkoxy, amino; E = cycloalkyl, alkyl, cycloalkylalkyl, hydroxyalkyl; R7R8 = O; R1R2 = (substituted) alkylene interrupted by O, S, SO2, imino], were prepd. Thus, title compd. (II) at 2×3 mg/kg orally in hamsters increased HDL levels by 9.21%.

IT **201848-96-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of condensed pyridines for treatment of hyperlipoproteinemia and arteriosclerosis)

RN 201848-96-6 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-cyclopentyl-4-(4-fluorophenyl)-6-[(phenylmethyl)amino]-, 5-ethyl 3-methyl ester (9CI) (CA INDEX NAME)



L11 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1996:427215 HCAPLUS
DOCUMENT NUMBER: 125:195564
TITLE: Approaches to combinatorial synthesis of heterocycles: solid phase synthesis of pyridines and pyrido[2,3-d]pyrimidines
AUTHOR(S): Gordeev, Mikhail F.; Patel, Dinesh V.; Wu, Jie; Gordon, Eric M.
CORPORATE SOURCE: Affymax Research Inst., Santa Clara, CA, 95051, USA
SOURCE: Tetrahedron Letters (1996), 37(27), 4643-4646
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 125:195564

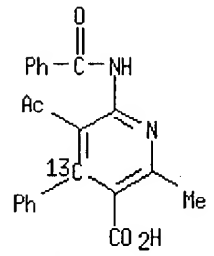
AB An efficient solid phase synthesis of diverse pyridines and pyrido[2,3-d]pyrimidines is described. An O-immobilized keto ester react with aldehydes to afford Knoevenagel derivs. These undergo hantzsch-condensation with α-oxo enamines to generate

1,4-dihydropyridines that are oxidized with CAN to produce immobilized pyridnes. The method has been extended to synthesis of fused pyrido[2,3-d]pyrimidines employing 6-aminouracils as the α-oxo enamine component. The course of the reaction on solid phase was studied by gel-phase 13C NMR spectroscopy. The synthesis is designed to be amenable for combinatorial libraries prepn.

IT **181033-90-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid phase synthesis of pyridines and pyridopyrimidines)

RN 181033-90-9 HCAPLUS

CN 3-Pyridine-4-13C-carboxylic acid, 5-acetyl-6-(benzoylamino)-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)



L11 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

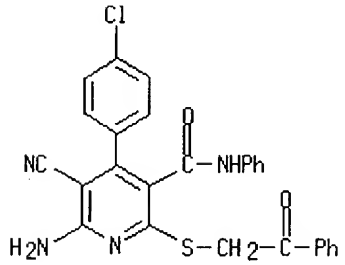
ACCESSION NUMBER: 1994:483000 HCAPLUS
DOCUMENT NUMBER: 121:83000
TITLE: New synthesis of polyfunctionally substituted 2-mercaptopyridines and fused pyridines
AUTHOR(S): Hussain, Sohair Mohamed; Sherif, Sherif Mourad; Youssef, Mohamed Mohamed
CORPORATE SOURCE: Faculty Sci., Cairo Univ., Giza, Egypt
SOURCE: Gazzetta Chimica Italiana (1994), 124(2), 97-101
CODEN: GCITA9; ISSN: 0016-5603
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 121:83000

AB Facile unequivocal syntheses of the title compds. are reported by reacting monothiomalonamide or its anilide analog with α-cyanocinnamonitriles.

IT **156643-98-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reactions of)

RN 156643-98-0 HCAPLUS

CN 3-Pyridinecarboxamide, 6-amino-4-(4-chlorophenyl)-5-cyano-2-[(2-oxo-2-phenylethyl)thio]-N-phenyl- (9CI) (CA INDEX NAME)



L11 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1974:108379 HCAPLUS
DOCUMENT NUMBER: 80:108379
TITLE: Pyridine derivatives
INVENTOR(S): Fleckenstein, Erwin; Heinrich, Ernst; Mohr, Reinhard
PATENT ASSIGNEE(S): Cassella Farbwerke Mainkur A.-G.
SOURCE: Ger. Offen., 93 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2230392	A1	19740131	DE 1972-2230392	19720622
NL 7308294	A	19731227	NL 1973-8294	19730614
JP 49062477	A2	19740617	JP 1973-69259	19730621
BE 801342	A1	19731226	BE 1973-132637	19730622
FR 2189402	A1	19740125	FR 1973-22862	19730622
FR 2189402	B1	19790302		
GB 1420987	A	19760114	GB 1973-29787	19730622
CH 610889	A	19790515	CH 1973-9107	19730622
US 3947463	A	19760330	US 1974-521530	19741106
US 3954782	A	19760504	US 1974-521408	19741106
US 3956294	A	19760511	US 1974-521443	19741106
US 3980659	A	19760914	US 1974-521442	19741106
US 3946024	A	19760323	US 1975-563848	19750331
FR 2330679	A1	19770603	FR 1976-16601	19760602
FR 2330679	B1	19790406		

PRIORITY APPLN. INFO.: DE 1972-2230392 19720622
US 1973-372024 19730621

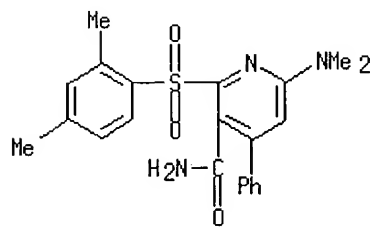
GI For diagram(s), see printed CA Issue.

AB Pyridine derivs. I (R and R1 = amino, alkoxy, alkylthio, CN, Cl) (642 compds.) were prepd. by substitution reactions on I (R = R1 = Cl).

IT **51566-40-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 51566-40-6 HCAPLUS

CN 3-Pyridinecarboxamide, 6-(dimethylamino)-2-[(2,4-dimethylphenyl)sulfonyl]-4-phenyl- (9CI) (CA INDEX NAME)



=> file caold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	64.08	221.39

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)        SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                   -6.93      -6.93

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FILE COVERS 1907-1966
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  display formats.

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=> d his

     (FILE 'HOME' ENTERED AT 00:42:09 ON 17 MAY 2004)

     FILE 'REGISTRY' ENTERED AT 00:42:16 ON 17 MAY 2004
L1              STRUCTURE UPLOADED
L2            0 S L1
L3           11 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 00:45:05 ON 17 MAY 2004
L4           10 S L3
L5            0 S L4 AND HOFFMAN, T?/AU
L6            0 S L4 AND POLI, S?/AU
L7            2 S L4 AND SCHNIDER, P?/AU
L8            8 S L4 NOT L7
L9            2 S L8 AND SLEIGHT, A?/AU
L10           2 S L9 NOT L7
L11           6 S L8 NOT L10

     FILE 'CAOLD' ENTERED AT 00:49:18 ON 17 MAY 2004

=> s l3
L12           0 L3

=>
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 NEWS  1            Web Page URLs for STN Seminar Schedule - N. America
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                    and searchable
 NEWS  4   JAN 27   A new search aid, the Company Name Thesaurus, available in
                    CA/CAplus
 NEWS  5   FEB 05   German (DE) application and patent publication number format
                    changes
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 NEWS 12   APR 26   PROMT: New display field available
 NEWS 13   APR 26   IFIPAT/IFIUDB/IFICDB: New super search and display field
                    available
 NEWS 14   APR 26   LITALERT now available on STN
 NEWS 15   APR 27   NLDB: New search and display fields available
 NEWS 16   May 10   PROUSDDR now available on STN
 NEWS 17   May 19   PROUSDDR: One FREE connect hour, per account, in both May
                    and June 2004
 NEWS 18   May 12   EXTEND option available in structure searching
 NEWS 19   May 12   Polymer links for the POLYLINK command completed in REGISTRY

 NEWS EXPRESS  MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
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FILE 'HOME' ENTERED AT 00:10:18 ON 17 MAY 2004

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

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=> file hcaplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.42	0.63

FILE 'HCAPLUS' ENTERED AT 00:11:18 ON 17 MAY 2004
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FILE COVERS 1907 - 17 May 2004 VOL 140 ISS 21
FILE LAST UPDATED: 16 May 2004 (20040516/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s neurokin? () receptor?
          4217 NEUROKIN?
        661192 RECEPTOR?
L1         896 NEUROKIN? (W) RECEPTOR?

=> s l1 and antagonist?
        207061 ANTAGONIST?
L2         547 L1 AND ANTAGONIST?

=> s l2 and modulat?
        286219 MODULAT?
L3          55 L2 AND MODULAT?

=> s l3 and disease?
        774818 DISEASE?
```

L4 6 L3 AND DISEASE?

=> d l4, ibib abs, 1-6

L4 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:499668 HCAPLUS
DOCUMENT NUMBER: 139:224911
TITLE: Enhancement of angiogenesis by endogenous substance P release and neurokinin-1 receptors during neurogenic inflammation
AUTHOR(S): Seegers, Helene C.; Hood, Vivienne C.; Kidd, Bruce L.; Cruwys, Simon C.; Walsh, David A.
CORPORATE SOURCE: Academic Rheumatology, City Hospital, University of Nottingham Clinical Sciences Building, Nottingham, UK
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2003), 306(1), 8-12
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Early angiogenesis is a key step in the transition from acute to persistent inflammation. The nervous system has long been known to play a role in inflammation, in part through the release of substance P from peripheral nerve terminals (neurogenic inflammation). Application of substance P can stimulate vessel growth in a variety of angiogenesis assays, although it was previously not known whether endogenous substance P released from sensory nerves could **modulate** angiogenesis. We hypothesized that endogenous substance P can initiate angiogenesis during acute neurogenic inflammation. Here we show that 10 nmol of substance P can stimulate angiogenesis within the rat knee synovium, as shown by increased endothelial cell proliferation index [PCNA index, 19% (95% confidence interval (CI), 17 to 20%)] compared with saline injected knees [6% (95% CI, 4% to 8%), $p < 0.05$]. Moreover, this was prevented by coadministration of an **antagonist** of the neurokinin-1 (NK1) subtype of **neurokinin receptor** SR140333 (nolpitantium), 1 μmol [8% (95% CI, 5% to 11%)]. Capsaicin 0.5%, which stimulates release of endogenous substance P from sensory nerves, was also found to enhance synovial angiogenesis, [PCNA index 17% (95% CI, 14% to 19%)] compared with saline injected control knees [2% (95% CI, 1% to 3%), $p < 0.05$], and this also was inhibited by 1 μmol of SR140333 [11% (95% CI, 8 to 16%)]. Inhibition of capsaicin-enhanced angiogenesis was incomplete, and this may indicate a contribution of other neuropeptides, in addn. to substance P-NK, receptor interactions, in capsaicin-enhanced angiogenesis. NK1 receptor **antagonists** could have therapeutic potential in conditions where neurogenic angiogenesis contributes to **disease**.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:879919 HCAPLUS
DOCUMENT NUMBER: 136:148995
TITLE: Role of spinal NMDA receptors, protein kinase C and nitric oxide synthase in the hyperalgesia induced by magnesium deficiency in rats
AUTHOR(S): Begon, Sophie; Pickering, Gisele; Eschalier, Alain;

Mazur, Andre; Rayssiguier, Yves; Dubray, Claude
CORPORATE SOURCE: EMI INSERM/UdA 9904 - Pharmacologie Fondamentale et Clinique de la Douleur, Laboratoire de Pharmacologie Medicale, Faculte de Medecine, Clermont-Ferrand, 63001, Fr.
SOURCE: British Journal of Pharmacology (2001), 134(6), 1227-1236
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 1 Magnesium (Mg)-deficient rats develop a mech. hyperalgesia which is reversed by a N-Methyl-D-Aspartate (NMDA) receptor **antagonist**. Given that functioning of this receptor-channel is **modulated** by Mg, we wondered whether facilitated activation of NMDA receptors in Mg deficiency state may in turn trigger a cascade of specific intracellular events present in persistent pain. Hence, we tested several **antagonists** of NMDA and non-NMDA receptors as well as compds. interfering with the functioning of intracellular second messengers for effects on hyperalgesia in Mg-deficient rats. 2 Hyperalgesic Mg-deficient rats were administered intrathecally (10 μl) or i.p. with different **antagonists**. After drug injection, pain sensitivity was evaluated by assessing the vocalization threshold in response to a mech. stimulus (paw pressure test) over 2 h. 3 Intrathecal administration of MgSO4 (1.6, 3.2, 4.8, 6.6 μmol) as well as NMDA receptor **antagonists** such as MK-801 (0.6, 6.0, 60 nmol), AP-5 (10.2, 40.6, 162.3 nmol) and DCKA (0.97, 9.7, 97 nmol) dose-dependently reversed the hyperalgesia. Chelerythrine chloride, a protein kinase C (PKC) inhibitor (1, 10.4, 104.2 nmol) and 7-NI, a specific nitric oxide (NO) synthase inhibitor (37.5, 75, 150 μmol kg-1, i.p.) induced an anti-hyperalgesic effect in a dose-dependent manner. SR-140333 (0.15, 1.5, 15 nmol) and SR-48968 (0.17, 1.7, 17 nmol), **antagonists** of **neurokinin receptors**, produced a significant, but moderate, increase in vocalization threshold. 4 These results demonstrate that Mg-deficiency induces a sensitization of nociceptive pathways in the spinal cord which involves NMDA and non-NMDA receptors. Furthermore, the data is consistent with an active role of PKC, NO and, to a lesser extent substance P in the intracellular mechanisms leading to hyperalgesia.

REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:152963 HCAPLUS
DOCUMENT NUMBER: 133:162890
TITLE: Substance P induction of murine keratinocyte PAM 212 interleukin 1 production is mediated by the neurokinin 2 receptor (NK-2R)
AUTHOR(S): Song, I.-S.; Bunnett, N. W.; Olerud, J. E.; Harten, B.; Steinhoff, M.; Brown, J. R.; Sung, K. J.; Armstrong, C. A.; Ansel, J. C.
CORPORATE SOURCE: Department of Dermatology, Emory University School of Medicine, Atlanta, GA, 30322, USA
SOURCE: Experimental Dermatology (2000), 9(1), 42-52
CODEN: EXDEEY; ISSN: 0906-6705
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The neurol. system plays an important role in **modulating** some

inflammatory skin **diseases**. Neuro-cutaneous interactions may be mediated by the release of neuropeptides such as substance P (SP) which activate immunocompetent cells in the skin by binding to high affinity **neurokinin receptors** (NKR). Since epidermal keratinocytes produce a variety of cytokines and are intimately assocd. with cutaneous sensory fibers, we tested the ability of these cells to participate in the cutaneous neuroimmune system by the secretion of potent cytokines such as interleukin 1 (IL-1) in response to released SP. RT-PCR studies demonstrated that cultured PAM 212 murine keratinocytes expressed mRNA for NK-2R but not NK-1R. Correspondingly, the addn. of SP to these cells resulted in a rapid increase in intracellular Ca2+ levels that could be specifically blocked by an NK-2R **antagonist**. NK-2R was also shown in normal mouse epidermis by immunohistochem. SP augmented the expression of PAM 212 keratinocyte IL-1α mRNA in a dose and time dependent manner and this induction was inhibited by an NK-2R **antagonist**. Secretion of bioactive IL-1α by the PAM 212 keratinocytes was likewise stimulated by SP in a dose dependent manner. These data support the hypothesis that SP released from cutaneous sensory nerves contributes to neuroimmune inflammatory responses in the skin by **modulating** the expression and release of cytokines from epidermal keratinocytes.

REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:305131 HCAPLUS
DOCUMENT NUMBER: 131:128572
TITLE: Role of neurokinin 3 receptors on responses to colorectal distention in the rat: electrophysiological and behavioral studies
AUTHOR(S): Julia, Veronique; Su, Xin; Bueno, Lionel; Gebhart, G. F.
CORPORATE SOURCE: Department of Pharmacology, College of Medicine, University of Iowa, Iowa City, IA, USA
SOURCE: Gastroenterology (1999), 116(5), 1124-1131
CODEN: GASTAB; ISSN: 0016-5085
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Tachykinins contribute to the control of gastrointestinal motility and **modulation** of somatic and visceral pain. The role of neurokinin (NK) B and NK3 receptors in visceral pain and gastrointestinal disorders has not been detd. Using electromyog. recordings of both abdominal and colonic muscle and electrophysiol. recordings of pelvic nerve afferent fibers, the authors studied drug effects on responses to colorectal distention. In awake rats, i.p. administration of the NK3-receptor **antagonist** SR 142,801 reduced, whereas the NK3-receptor agonist senktide increased, both the rectocolonic inhibitory reflex and abdominal contractions produced by colorectal distention. In contrast, intracerebroventricular administration of SR 142,801 increased the no. of abdominal contractions without affecting the rectocolonic inhibitory reflex produced by colorectal distention. In a similar manner, intracerebroventricular injection of senktide diminished the no. of abdominal contractions. In electrophysiol. expts., SR 142,801 decreased responses of pelvic nerve afferent fibers to colorectal distention. Responses of pelvic nerve fibers to urinary bladder distention, however, were unaffected by SR 142,801. These results suggest that peripheral NK3 receptors are involved in the mediation of both visceral nociception and gastrointestinal disorders. Also, central NK3 receptors seem to play a role in the

modulation of visceral nociception.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References

ACCESSION NUMBER: 1994:474388 HCAPLUS
DOCUMENT NUMBER: 121:74388
TITLE: Involvement of spinal tachykinin NK1 and NK2 receptors in detrusor hyperreflexia during chemical cystitis in anesthetized rats
AUTHOR(S): Lecci, Alessandro; Giuliani, Sandro; Santicioli, Paolo; Maggi, Carlo Alberto
CORPORATE SOURCE: Pharmacology Research Department Menarini' Pharmaceuticals, Via Sette Santi 3, Florence, 50131, Italy
SOURCE: European Journal of Pharmacology (1994), 259(2), 129-35
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The i.p. administration of cyclophosphamide (150 mg/kg, 48 h before cystometry) induced detrusor hyperreflexia in urethane-anesthetized rats. Intrathecal (i.t.) administration of the selective tachykinin NK1 receptor **antagonist**, GR 82334 ([D- Pro9(spiro-γ-lactam)Leu10,Trp11]physalemin-(1-11)) (1 nmol/rat i.t.) had no significant effect on micturition in normal rats but increased the vol. threshold in cyclophosphamide-treated rats. Another tachykinin NK1 receptor **antagonist**, RP 67580 ((3aR,7aR)-7,7-diphenyl-2-[1-imino-2(2-methoxyphenyl)ethyl]perhydroisoindol-4-one) (10 nmol/rat i.t.) increased the vol. threshold to a similar extent in both vehicle- and cyclophosphamide-treated animals. The tachykinin NK2 receptor **antagonist**, SR 48968 (S7-N-methyl-N[4- (acetylamino-4-phenylpiperidino)-2-(3,4-dichlorophenyl)butyl]benzamide hydrochloride) (10 nmol/rat i.t.) did not modify micturition parameters in normal rats but antagonized bladder hyperreflexia in cyclophosphamide-treated animals; SR 48968 restored the vol. threshold for the micturition reflex to values close to control values. SR 48965 (R7-N-methyl-N[4-(acetylamino-4-phenylpiperidino)-2-(3,4- dichlorophenyl)butyl]benzamide hydrochloride) (10 nmol/rat i.t.), the enantiomer of SR 48968 devoid of affinity for tachykinin NK2 receptors, was inactive. 2-Amino-5- phosphonovaleric acid (25 and 250 nmol/rat i.t.), a selective **antagonist** of NMDA receptors, augmented the vol. threshold both in controls and in rats with detrusor hyperreflexia; after administration of this **antagonist**, however, the vol. threshold in cyclophosphamide-treated animals was still lower than in controls. I.v. administration of SR 48968, RP 67580, or the combined administration of SR 48968 and RP 67580 had no effect on cystometry variables either in rats with detrusor hyperreflexia or in controls. Apparently, tachykinin NK1 and NK2 receptors located in the spinal cord are involved in bladder hyperreflexia caused by chem. induced cystitis.

L4 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References

ACCESSION NUMBER: 1993:663320 HCAPLUS
DOCUMENT NUMBER: 119:263320
TITLE: Tachykinin-mediated respiratory effects in conscious guinea pigs: **Modulation** by NK1 and NK2 receptor **antagonists**

AUTHOR(S): Kudlacz, Elizabeth M.; Logan, Deborah E.; Shatzer, Scott A.; Farrell, Amy M.; Baugh, Larry E.
CORPORATE SOURCE: Marion Merrell Dow Res. Inst., Cincinnati, OH, 45215, USA
SOURCE: European Journal of Pharmacology (1993), 241(1), 17-25
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Tachykinins, in particular neurokinin A and substance P, produce a no. of airway effects which may contribute to respiratory **diseases** such as asthma. The authors examd. the ability of aerosolized substance P, neurokinin A or capsaicin to produce respiratory alterations in conscious guinea pigs using modified whole body plethysmog. Substance P-mediated dyspnea and significant respiratory events were inhibited by the NK1 receptor **antagonist** CP-96,345. Neurokinin A-mediated respiratory effects were ablated by the NK2 receptor **antagonists**: MEN 10207, MDL 29,913 and SR 48,968, the latter being the most potent. The peptide-based **antagonist**, MEN 10207, produced respiratory effects itself, suggesting partial agonist activity. The cyclic hexapeptide, MDL 29,913, relaxed airway smooth muscle via mechanisms other than tachykinin antagonism. NK2 but not NK1 receptor **antagonists** were able to delay the onset of capsaicin-induced dyspnea, although alone they did not usually (in approx. 10% of the animals) eliminate the response. However, when NK2 receptor **antagonists** were combined with CP-96,345, the incidence of dyspnea induced by capsaicin decreased significantly (40%) suggesting that both tachykinins contribute to dyspnea in this system.

=> d his

(FILE 'HOME' ENTERED AT 00:10:18 ON 17 MAY 2004)

FILE 'REGISTRY' ENTERED AT 00:10:33 ON 17 MAY 2004

FILE 'HCAPLUS' ENTERED AT 00:11:18 ON 17 MAY 2004
L1 896 S NEUROKIN? () RECEPTOR?
L2 547 S L1 AND ANTAGONIST?
L3 55 S L2 AND MODULAT?
L4 6 S L3 AND DISEASE?

=> s l4 and dt/review
'REVIEW' IS NOT A VALID FIELD CODE
0 DT/REVIEW
L5 0 L4 AND DT/REVIEW

=> s l4 and review/dt
1726332 REVIEW/DT
L6 0 L4 AND REVIEW/DT

=> s l3 and review/dt
1726332 REVIEW/DT
L7 2 L3 AND REVIEW/DT

=> d l7, ibib abs, 1-2

L7 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:662232 HCAPLUS
DOCUMENT NUMBER: 137:210302

TITLE: Generalized anxiety disorder: treatment options
AUTHOR(S): Sramek, John J.; Zarotsky, Victoria; Cutler, Neal R.
CORPORATE SOURCE: Ingenix Pharmaceutical Services, Beverly Hills, CA, USA
SOURCE: Drugs (2002), 62(11), 1635-1648
CODEN: DRUGAY; ISSN: 0012-6667
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. In recent years generalized anxiety disorder (GAD) has become a much better defined disorder, with specific criteria distinguishing it from the other anxiety disorders; however, it still lacks the same public and scientific interests as some of the other anxiety disorders such as panic and social phobia. Nevertheless, refinement in the treatment of GAD is becoming more evident through the conduct of clin. trials. Up until the mid-1980's, treatment consisted primarily of benzodiazepines. However, as a result of growing characterization of their abuse potential, other therapeutic options were explored. Benzodiazepines became seen as an effective short-term therapy, and buspirone and some of the newer antidepressants have become the treatment of choice for patients with GAD requiring long-term treatment. Buspirone was the first available alternative to the benzodiazepines in the US; however, the initial excitement over this agent was somewhat dampened because of its mild efficacy combined with a slow onset of action. The antidepressants were seen as beneficial for the treatment of GAD because of the high comorbidity with depression, thus allowing a better outcome for these patients. The antidepressants that offer both a good adverse effect profile and efficacy are the selective serotonin reuptake inhibitors including paroxetine, and the serotonin-norepinephrine reuptake inhibitors such as venlafaxine. Clinicians should also consider the potential benefits of psychotherapy as an adjunct to medication. There are a no. of potentially new pharmacotherapies being investigated, including newer serotonin 5-HT1A receptor agonists, cholecystokinin receptor **antagonists**, **neurokinin receptor antagonists**, gabapentin and its analogs, and γ-aminobutyric acid (GABA)A receptor **modulators**. However, these compds. are all in the early stages of investigation, and there are no new therapies expected to be released in the near future. Nonetheless, in the search for the ideal anxiolytic, a more pos. outlook is allowed by imminent future research for new treatment options in patients with GAD.

REFERENCE COUNT: 103 THERE ARE 103 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:41229 HCAPLUS
DOCUMENT NUMBER: 128:175662
TITLE: **Neurokinin receptor antagonists**: therapeutic potential in the treatment of pain syndromes
AUTHOR(S): Sakurada, Tsukasa; Sakurada, Chikai; Tan-No, Koichi; Kisara, Kensuke
CORPORATE SOURCE: Department of Biochemistry, Daiichi College of Pharmaceutical Sciences, Fukuoka, Japan
SOURCE: CNS Drugs (1997), 8(6), 436-447
CODEN: CNDREF; ISSN: 1172-7047
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 155 refs. The involvement of tachykinin neuropeptides, such as substance P and the neurokinins, in pain transmission is supported by a wealth of evidence. At present, the therapeutic potential of manipulating tachykinin-mediated effects is being investigated and has been assisted by the discovery of several nonpeptide, metabolically stable compds. that are **antagonists** at neurokinin (NK) receptors. Since multiple neurotransmitters or neuromodulators are involved in nociception in primary afferents, drugs that are **antagonists** at both tachykinin NK1 and NK2 receptors could be clin. more useful than receptor-selective drugs in the treatment of pain syndromes. NK1 receptor **antagonists** that are also opioid receptor agonists, or the combination of **neurokinin receptor antagonists** with opioids, may also be promising approaches to treating pain.

REFERENCE COUNT: 155 THERE ARE 155 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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